Remarks

The June 30, 2011 Official Action has been carefully reviewed. In view of the following remarks, favorable reconsideration and allowance of this application are respectfully requested.

At the outset it is noted that a shortened statutory response period of three (3) months was set forth in the June 30, 2011 Official Action. Therefore, the initial due date for response was September 30, 2011. Accordingly, a petition for a 2 month extension is presented with this response, which is being filed within the two month extension period.

As a preliminary matter, Applicants note that the Office Action Summary indicates that the instant Official Action is Final. This is incorrect. Indeed, at page 2 of the Official Action, the Examiner states that the finality of the previous Official Action had been withdrawn. Further, the Patent Application Information Retrieval (PAIR) system clearly indicates that the instant Official Action is non-Final. Accordingly, it is evident that the box 2a) was improperly ticked on the Office Action Summary and that box 2b) should have been marked.

Claims 1, 9, 13, 17, 20, 25, 29, and 34-37 have been rejected under 35 U.S.C. §102(b) as allegedly anticipated by U.S. Patent 6,323,219 (Costanzo).

Claims 1-4, 9, 13, 17-20, 25, 29, and 34-41 have been rejected under 35 U.S.C §103(a) for allegedly unpatentable over the '219 patent.

Lastly, the Examiner has rejected claims 1-4, 9, 13 17-20, 25, 29, and 34-41 under 35 U.S.C §103(a) as allegedly unpatentable over U.S. Patent 4,906,457 (Ryan) in view of Japanese Patent Application 07010772 (Madea et al.).

The foregoing rejections constitute all of the grounds set forth in the June 30, 2011 Official Action for refusing the present application.

No new matter has been introduced into this application by reason of any of the amendments presented

herewith.

In view of the present amendment and the reasons set forth in this response, Applicants respectfully submit that the 35 U.S.C. §102(b) rejection 1, 9, 13, 17, 20, 25, 29, and 34-37 and the 35 U.S.C. §103(a) rejections of claims 1-4, 9, 13, 17-20, 25, 29, and 34-41, as set forth in the June 30, 2011 Official Action, cannot be maintained. These grounds of rejection are, therefore, respectfully traversed.

CLAIMS 1, 9, 13, 17, 20, 25, 29 AND 34-37 ARE NOT ANTICIPATED BY THE '219 PATENT

Claims 1, 9, 13, 17, 20, 25, 29, and 34-37 have been rejected under 35 U.S.C. §102(b) as allegedly anticipated by U.S. Patent 6,323,219. The '219 patent allegedly discloses a preparation of STI by grinding soybean in purified water and the application of the STI composition to the skin of swine. It is the Examiner's position that any application on the above STI composition to skin would read on the instant methods. Applicants respectfully disagree with the Examiner's position.

The '219 patent (which was co-invented by Miri Seiberg, one of the co-inventors of the instant application) does not teach or suggest the use of a non-denatured, Kunitz-type soybean trypsin inhibitor for reducing the risk of developing a cutaneous tumor, as instantly claimed. Rather, the '219 patent is concerned with "compounds which affect melanogenesis and can be used as depigmenting agents" (see Abstract).

Claims 1 and 17 of the instant invention, from which the other claims depend, recite the topical application of a composition comprising non-denatured, soy product comprising a non-denatured, Kunitz-type soybean trypsin inhibitor "***prior*** to exposure of the skin to ultraviolet radiation." Accordingly, the instant claims recite the application of the composition *followed* by exposure to ultraviolet irradiation. In stark contrast, the '219 patent demonstrates the application of

their STI composition *after* ultraviolet application. Indeed, at column 8, lines 32-50, the '219 patent states that STI application would be useful to reduce pigmentation. Further, at column 12, lines 66-67, the '219 patent states that STI was "very effective in inhibiting melanogenesis." As shown in Figure 4B, the '219 patent demonstrates that exposure of skin cells to UVB irradiation increased melanogenesis and pigmentation. Subsequent application of a trypsin inhibitor resulted in the depigmentation of the skin *already* exposed to UVB irradiation.

"To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such a gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is **necessarily** present in the thing described in the reference." *Continental Can C. USA v. Monsanto Co.*, 20 U.S.P.Q.2d 1746, 1749 (Fed. Cir. 1991). Furthermore, as set forth in MPEP §2112, "The fact that a certain result or characteristic may occur or be present in the prior art is NOT sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 28 U.S.P.Q.2d 1955, 1957 (Fed. Cir. 1993)." "Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is NOT sufficient." *In re Robertson*, 49 U.S.P.Q.2d 1949, 1950-51, (Fed. Cir. 1999).

Furthermore, there is considerable precedent, including cases factually analogous to the present facts, that supports Applicants' position that the '219 patent does not constitute an anticipation of the claims against which they are cited. For example, in *In re Marshall*, 198 U.S.P.Q. 344 (C.C.P.A. 1978), the Court of Customs and Patent Appeals reversed a §102 rejection of claims directed to a weight control process using a oxethazine which was previously taught by the Physicians' Desk reference (PDR) to be effective for the treatment of esophagitis, gastritis, peptic ulcer, and

irritable colon syndrome. The rationale for the Court's decision was simply stated as follows:

> "Nothing in the PDR remotely suggests taking oxethazine to lose weight. If anyone ever lost weight by following the PDR teachings it was an unrecognized accident. **An accidental or unwitting duplication of an invention cannot constitute an anticipation.**" [Citation omitted; Emphasis added].

Notably, this result is consistent with the reasoning of the U.S. Supreme Court which stated in *Tilghman v. Proctor*, 102 U.S. 707 (1881), that if a compound was "accidentally and unwittingly produced, whilst the operators where in pursuit of other and different results, without exciting attention and without it being known what was done or how it had been done, it would be absurd to say that this was an anticipation."

A similar outcome was reached in *Rapoport v. Dement*, 59 U.S.P.Q.2nd 1215 (Fed. Cir. 2001), an interference in which the subject matter at issue was a method for the treatment of sleep apnea. More specifically, the interference count called for treating sleep apnea by administering a therapeutically effective amount of certain azapirone compounds, such as buspirone. The PTO Board of Appeals found that a prior publication disclosing the use of buspirone to treat anxiety in patients suffering from sleep apnea did not disclose administration of buspirone for the treatment of patients suffering from sleep apnea, *per se*. This determination was sustained on appeal to the Federal Circuit. The Board's decision and the Federal Circuit's affirmance thereof were based on the finding that treatment of the sleep apnea disorder itself is distinct from treatment of anxiety and other secondary symptoms related to sleep apnea. This finding was, in turn, based on the interpretation that the claim terminology "treatment of sleep apneas" should be treated as a **claim limitation**. Because the cited prior art publication failed to disclose treatment of the underlying sleep apnea disorder, as opposed to the symptoms thereof, it was held not

to anticipate the count. Indeed, the Federal Circuit observed in this regard that there was no disclosure in the publication of tests in which buspirone was administered to patients suffering from sleep apnea "with the intent to cure the underlying condition." Id. at 1221.

Notably, the Federal Circuit confirmed the above finding in *Rapoport* in *Jansen v. Rexall Sundown, Inc.*, 342 F.3d 1329, 68 U.S.P.Q.2D 1154 (Fed. Cir. 2003). In *Jansen*, the Federal Circuit stated that when a preamble gives "life and meaning" to the claim, the preamble is "not merely a statement of effect that may or may not be desired or appreciated. Rather, it is a statement of the intentional purpose for which the method must be performed." As such, the claims were "interpreted to require that the method be practiced with the intent to achieve the objective stated in the preamble."

In view of the foregoing authorities, the conclusion is inescapable that the '219 patent fails to disclose a method for reducing the risk of cutaneous tumor development or reducing the risk of ultraviolet radiation-induced skin cancer, as recited in the instant claims. In this case, as in *Rapoport*, there is no disclosure in the cited prior art of the administration of a composition comprising a non-denatured, Kunitz-type soybean trypsin inhibitor for reducing the risk of cutaneous tumor development or reducing the risk of ultraviolet radiation-induced skin cancer. Further, the connection in the instant case between the prior art and the claimed method is clearly more attenuated in the instant case than in *Rapoport*. Indeed, the prior art in *Rapoport* involved the treatment of a symptom of a condition and the claims were drawn to the treatment of the condition itself. Here, the '219 patent exemplifies treating skin *after* UV irradiation whereas the instantly claimed invention requires topical application of a composition comprising a non-denatured, Kunitz-type soybean trypsin inhibitor *prior* to UV irradiation.

In addition to the foregoing, the '219 patent

teaches that soybean trypsin inhibitor (STI) is effective in inhibiting melanogenesis, the process by which melanin is made. As of the effective filing date of the instant application, the skilled artisan understood melanin provided protection for skin from harmful ultraviolet radiation. For example, Gilchrest et al. (N. Eng. J. Med. (1999) 340:1341-1348) teach that "poorly melanized skin is far more vulnerable than melanized skin to acute and chronic injury caused by ultraviolet radiation (sunburn and photoaging or *photocarcinogenesis*...)" (page 1343, left column; emphasis added). Gilchrest et al. further state that melanin "has a photoprotective function in the skin, directly absorbing ultraviolet photons as well as reactive oxygen species generated by the interaction of ultraviolet photons with membrane lipids and cellular chromophores" (page 1343, left column). Notably, melanin levels are increased in response to ultraviolet injury of skin which results in "a long-lasting endogenous "sunscreen" with a measured sun protection factor of approximately 3 to 5" (page 1343, left column). Moreover, other studies have shown that the increased levels of melanin in dark skin reduces the amount of ultraviolet radiation that reaches the upper dermis 5 fold and reduces the risk of skin cancer 500-1000 fold when compared to Caucasian skin (see, e.g., the abstracts of Kaidbey et al. (J. Am. Acad. Dermatol. (1979) 1:249-260) and Kollias et al. (J. Photochem. Photobiol. B. (1991) 9:135-160)). In view of the foregoing, it is evident that the skilled artisan understood that increased melanin levels protected skin from ultraviolet radiation and reduced cutaneous tumor and skin cancer development. However, the '219 patent teach that STI administration *decreases* the levels of pigmentation and melanin, thereby teaching away from the instantly claimed invention. In view of the above, a skilled artisan - apprised of the '219 patent - could **not** have determined/anticipated that the administration of non-denatured, soy products comprising non-denatured, Kunitz-type soybean trypsin inhibitor would have decreased the risk of

cutaneous tumor development in skin cells, as instantly claimed. Indeed, based on the above references, a skilled artisan clearly would have *avoided* applying depigmenting agents - such as STI as taught by the '219 patent - prior to exposure of UV irradiation.

In view of all of the foregoing, Applicants respectfully submit that the instant rejection under 35 U.S.C. §102(b) is untenable. Withdrawal of the rejection is respectfully requested.

CLAIMS 1-4, 9, 13, 17-20, 25, 29 AND 34-41 ARE NOT RENDERED OBVIOUS BY THE '219 PATENT

Claims 1-4, 9, 13, 17-20, 25, 29, and 34-41 have been rejected under 35 U.S.C §103(a) for allegedly unpatentable over the '219 patent. It is the Examiner's position that even though the '219 patent does not specifically disclose administering STI compositions to cells which have not been damaged by UV radiation, it allegedly would have been obvious to do so as unwanted skin pigmentation may occur in skin that has not been exposed to UV radiation. Applicants respectfully disagree with the Examiner's position for the reasons set forth above with regard to the 35 U.S.C §102 rejection and those set forth below.

As stated hereinabove, the instant claims recite application of a composition comprising a non-denatured, Kunitz-type soybean trypsin inhibitor "***prior*** to exposure of the skin to ultraviolet radiation." In contrast, the '219 patent teaches applying STI compositions to already pigmented skin (e.g., ***after*** skin has been exposed to UV radiation). Further, as explained hereinabove, it was well known as of the effective filing date of the instant application that melanogenesis and *increased* melanin levels protected skin from ultraviolet radiation and reduced cutaneous tumor and skin cancer development. However, in stark contrast, the '219 patent teaches that STI compositions are inhibitors of

melanogenesis and *reduce* melanin levels. This is a *direct teaching away* from the instantly claimed methods. Indeed, in view of the above, a skilled artisan - apprised of the '219 patent - would have determined that the administration of an STI would have ***increased*** the risk of cutaneous tumor development in skin cells, in complete contrast to the instantly claimed methods.

Inasmuch as the reference cited by the Examiner directly teaches away from the instantly claimed invention, it is self-evident that the instant obviousness rejection cannot be reasonably maintained. Withdrawal of the rejection is respectfully requested.

CLAIMS 1-4, 9, 13, 17-20, 25, 29 AND 34-41 ARE NOT RENDEREDED OBVIOUS BY THE '457 PATENT IN VIEW OF THE '772 APPLICATION

Claims 1-4, 9, 13, 17-20, 25, 29, and 34-41 have been rejected under 35 U.S.C §103(a) for allegedly unpatentable over the '457 patent in view of the '772 application. The '457 patent allegedly discloses the topical administration of soybean trypsin inhibitors for reducing the risk of skin cancer caused by sunlight or other ultraviolet radiation. The '772 application allegedly teach that soybean trypsin inhibitors include Kunitz-type soybean trypsin inhibitors. It is the Examiner's position that it would have been obvious to a skilled artisan to combine the above disclosures to arrive at the instantly claimed invention.

Applicants respectfully disagree with the Examiner's position for the reasons of record and those set forth below.

At page 7 of the instant Official Action, the Examiner states that "while the references of Hunag et al., Kennedy, Yavelow and Messina do not direct the skilled artisan to the use of a trypsin inhibitor, ... the skilled artisan would be motivated to select a trypsin inhibitor ... based on the prior art reference which teaches their use. Applicants respectfully disagree with the Examiner's position.

35 U.S.C. §103(a) states:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious ***at the time the invention was made*** to a person having ordinary skill in the art to which said subject matter pertains. (Emphasis added.)

It is also a well-settled premise of patent law that the "person of ordinary skill in the art at the time of the patentee's invention ... is presumed to have before him *all of the relevant prior art.*" *Orthopedic Equip. Co. v. United States*, 702 F.2d 1005, 1012, 217 USPQ 193 (Fed. Cir. 1983) (Emphasis added). Applicants respectfully submit that the relevant prior art clearly fails to render the instantly claimed invention obvious. Indeed, the prior art, when considered as a whole, clearly teach away from the instantly claimed invention.

The '457 patent only teaches the use of "chymotrypsin and trypsin families of protease inhibitors" and only specifically exemplifies the use of the soybean-derived Bowman-Birk inhibitor (BBI; see paragraph bridging columns 1 and 2). Indeed, the '457 patent states that the "soybean-derived Bowman Birk inhibitor family ... [is an appropriate family] of inhibitors for use in the novel compositions and methods of this invention" (column 2, lines 3-6). Moreover, the only soybean product exemplified by the '457 patent is the Bowman-Birk inhibitor, which inhibits chymotrypsin and trypsin (see Example 2). It is also noteworthy that the other "chymotrypsin and trypsin" family of protease inhibitors listed by the '457 patent is potato inhibitor 1 family (column 2). As with the Bowman Birk inhibitor family, the potato inhibitor 1 family of proteases inhibits chymotrypsin. Therefore, the '457 patent only teaches the anti-cancer properties of chymotrypsin inhibitors and fails to teach or suggest the use of a trypsin specific inhibitor, such as the instantly claimed Kunitz-type soybean trypsin inhibitor.

As acknowledged by the Examiner at page 5 of the

instant Official Action, the '457 patent fails to specifically teach using the non-denatured, Kunitz-type soybean trypsin inhibitor of the instantly claimed invention.

The other reference relied on by the Examiner, the '772 application, only discloses that the Kunitz-type soybean trypsin inhibitor suppresses increased inflammatory edema. There is no teaching or suggestion that the Kunitz-type soybean trypsin inhibitor reduces the risk of cutaneous tumor development in skin cells that have not yet been damaged by ultraviolet radiation or reduces the risk of ultraviolet radiation-induced skin cancer in skin cells that have not been damaged by ultraviolet radiation, when administered topically, as instantly claimed. It appears that the Examiner relies on the '772 application only as evidence of the existence of a soybean Kunitz-type trypsin inhibitor.

Accordingly, the '772 application provides no further motivation to a skilled artisan to select non-denatured, Kunitz-type soybean trypsin inhibitor to use in methods of reducing the risk of cutaneous tumor development in skin cells or reducing the risk of ultraviolet radiation-induced skin cancer, as instantly claimed.

In stark contrast, the prior art is replete with teachings that - in the context of soybeans - the cancer inhibitor is the Bowman Birk inhibitor (which inhibits chymotrypsin and trypsin as advocated by the '457 patent) and **not** the Kunitz-type soybean trypsin inhibitor. As explained - in part - in previous Official Action responses, the following references (most of which were published ***after*** the '457 patent) all clearly teach away from the instantly claimed invention:

1) Huang et al. (Proc. Natl. Acad. Sci. (1997) 94:11957-11962; previously submitted) teach that "solar UV irradiation is the causal factor for the increasing incidence of human skin carcinomas [and that] the activation of the transcription factor activator protein-1 (AP-1) has been shown to be responsible for the tumor promoter action of UV light"

(Abstract). Huang et al. demonstrate that while chymotrypsin inhibitors are capable of inhibiting the UV-activation of AP-1, trypsin inhibitors, such as the soybean trypsin inhibitor, are completely *incapable* of inhibiting AP-1 activation by ultraviolet radiation.

2) Kennedy, A.R. (Amer. J. Clin. Ntr. (1998) 68:1406S-1412S; previously submitted) clearly states that "the ability to inhibit carcinogenesis is associated with the ability to inhibit chymotrypsin" (page 1407S). Further, Kennedy state that "the active anticarcinogenic activity has been shown to be chymotrypsin inhibitor activity, which is present in soybeans ***only*** in BBI" (page 1407S; emphasis added). Thus, it was clearly understood by those in the art that only chymotrypsin inhibitors - such as BBI, but not Kunitz-type trypsin inhibitors - inhibited carcinogenesis.

3) Yavelow et al. (Proc. Natl. Acad. Sci. (1985) 82:5395-5399; previously submitted) state that "other soybean protease inhibitors ... lack the ability to suppress transformation *in vitro*" (page 5395). Yavelow et al. further state that the "Kunitz soybean trypsin inhibitor, which inhibits primarily trypsin, has ***no effect*** on radiation-induced transformation" (page 5398; emphasis added).

4) Messina et al. (J. Natl. Cancer Inst. (1991) 83:541-546; previously submitted) teach that "comparisons of the pure BBI with an extract of soybeans containing BBI indicate that the activity of the soybean extract could be ***directly attributable to BBI***" (page 542; emphasis added).

5) U.S. Patent 5,961,980 states that "protease inhibitors specific for chymotrypsin, but not those that are trypsin-specific, are capable of inhibiting formation of active oxygen species," which are known to contribute to carcinogenicity (at column 3, lines 1-20).

6) Kennedy, A.R. (Cancer Research (1994) 54:1999s-2005s) teach that while "protease inhibitors can almost be considered "universal" anticarcinogenic agents", they found that "BBI was the ***only compound in soybeans*** with the ability to suppress *in*

vitro transformation" and that the chymotrypsin inhibitory properties of BBI, *but not its trypsin inhibitory activity*, is involved in the suppression of transformation and carcinogenesis (pages 1999s and 2004s).

Accordingly, in view of all of the foregoing, a skilled artisan *at the time of the instant invention* understood that the anti-cancer properties of soy were solely attributable to chymotrypsin inhibitors and not trypsin specific inhibitor, such as the instantly claimed Kunitz-type soybean trypsin inhibitor. The '457 patent does not specifically direct the skilled artisan to the non-denatured, Kunitz-type soybean trypsin inhibitor, as instantly claimed. The '772 application, cited by the Examiner, also fails to direct the skilled artisan to the non-denatured, Kunitz-type soybean trypsin inhibitor for reducing the risk of developing cancer. However, all of the above cited references directly teach the skilled artisan that - in the specific context of soy - the anti-carcinogenesis properties lie with the chymotrypsin inhibitor properties of the Bowman-Birk inhibitor. The skilled artisan would have had no motivation and no expectation of success - at the time of the instant invention - to use non-denatured, Kunitz-type soybean trypsin inhibitor in the instantly claimed methods. Indeed, the '457 patent merely provides a large genus of inhibitors and only shows the efficacy of certain chymotrypsin inhibitors. However, the above cited references speak to the specific genus of soybean inhibitors and unmistakably teach the skilled artisan that the only anti-cancer properties lie with BBI.

Notably, in *Eli Lilly & Co. v. Teva Pharms. United States, Inc.*, 657 F. Supp. 2d 967 (S.D. Ind. 2009), the obviousness of a patent claiming low dose administration of raloxifene for the treatment of osteoporosis was disputed. The prior art allegedly taught the use of tamoxifen and analogs thereof for the treatment of osteoporosis. Raloxifene is an analog of tamoxifen. However, the Court stated that "the evidence adduced at trial here showed that, *at the time*

of the invention, significant concerns regarding raloxifene's bioavailability led to the belief that a large dose of the drug would be necessary to be effective, and thus, that a person of ordinary skill in the art would not have a reasonable expectation of success in using such a low dose of raloxifene." (Emphasis in original). The Court held that the claims reciting low dose administration were not rendered obvious by the prior art in view of this further understanding at the time of the invention.

In the instant case, the Examiner asserts that the '457 patent has broadly taught that "chymotrypsin and trypsin families of protease inhibitors families of protease inhibitors derived from plants, such as from potatoes and soybeans" may be used for reducing the risk of skin cancer. However, there is no particular teaching in the '457 patent or the '772 application to use non-denatured, Kunitz-type soybean trypsin inhibitor, as instantly claimed. In contrast, the art available to the skilled artisan at the time of the instant invention clearly teaches that - in the context of soybeans - the anti-carcinogenesis properties are contained solely within in the chymotrypsin inhibitor BBI. Accordingly, the skilled artisan, apprised of the prior art, would understand that the "chymotrypsin and trypsin families of protease inhibitors families of protease inhibitors derived from plants, such as from potatoes and soybeans" of the '457 patent does **not** include non-denatured, Kunitz-type soybean trypsin inhibitor, as instantly claimed.

For the foregoing reasons, Applicants respectfully submit that the Examiner has failed to establish a prima facie case of obviousness and that the instant rejection under 35 U.S.C. §103 cannot be reasonably maintained.

At page 7 of the instant Official Action, the Examiner states that at 21 weeks, "while the soymilk treatment reduced the percentage [of mice with tumors] to 83%, heated soymilk and BBI also reduced the percentage of mice with tumors to 90%." The Examiner further states that "it is

unclear if the results are unexpected or simply due to the combination effect of the combined protease inhibitors." Applicants respectfully disagree. In Figure 1A, liposomes comprising STI were better than liposomes comprising BBI in reducing the number of mice with tumors. Inasmuch as the only difference between to the two treatment methods is STI vs. BBI, it can be stated that the benefit in treatment is attributable to STI. Accordingly, as demonstrated in Figures 1, 2, and 4 and Table 1 of U.S. Patent Application No. 10/108,248 the Kunitz-type soybean trypsin inhibitor is as effective, if not more effective, at inhibiting tumor formation than BBI. Moreover, Example 4 of the instant application demonstrates that the Kunitz-type soybean trypsin inhibitor, when applied to swine skin, reduced, if not eliminated, DNA damage (thymidine dimer formation) caused by ultraviolet radiation. This finding was neither taught nor suggested by the prior art and is an unexpectedly superior finding over the understanding in the art at the time of the instant invention.

In view of the foregoing, it is clear that the instant rejection of claims 1-4, 9, 13, 17-20, 25, 29, and 34-41 under 35 U.S.C §103(a) is untenable. Withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the foregoing amendment and remarks, it is respectfully urged that the rejections set forth in the June 30, 2011 Official Action be withdrawn and that this application be passed to issue.

In the event the Examiner is not persuaded as to the allowability of any claim, and it appears that any outstanding issues may be resolved through a telephone interview, the Examiner is requested to telephone the undersigned attorney at the phone number given below.

If a fee is required or an overpayment is made, the Commissioner is authorized to charge or credit the deposit

account of the undersigned, Account No. 04-1406.

Respectfully submitted,
DANN, DORFMAN, HERRELL AND SKILLMAN
A Professional Corporation

By _____
Robert C. Netter, Jr., Ph.D., J.D.
PTO Registration No. 56,422

Telephone: (215) 563-4100
Facsimile: (215) 563-4044
Enclosures: Kennedy, A.R., Cancer Research (1994) 54:1999s-2005s